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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Yoshio Jo, et al.	Group Art Unit: 1615
Serial No:	10/069,561	Examiner: Oh, Simon J.
Filed:	October 22, 2001	Dated: May 19, 2004
For:	**SOLUBLE TRAUMA-HEALING HEMOSTATIC CELLULOSE**	

Commissioner for Patents
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DECLARATION

I, Yoshio Jo, do hereby declare:

1. I am one of the joint inventors of the invention being claimed in the above-identified patent application;

2. I have read and understand the Office Action mailed January 27, 2004 by the Patent and Trademark Office in the above-identified application and the art being applied therein, namely European Pat. Appln. No. 0956869 (an equivalent to U.S. Pat. No. 6,200,587 to Soe et al.), U.S. Pat. No. 4,340,731 to Colombo et al., U.S. Pat. No. 5,962,026 to Edwardson et al. and U.S. Pat. No. 4,265,233 to Sugitachi et al. (hereinafter referred to as "Soe et al.", "Colombo et al.", "Edwardson et al." and "Sugitachi et al.");

3. The present invention, provides distinct and important improvement in manufacturing a soluble trauma-healing hemostatic cellulose fiber containing coagulation

proteins and which rapidly dissolves when contacting blood to provide excellent hemostatic effect, especially in a large amount of blood such as a wound. More particularly, the claimed hemostatic fiber exhibits the important hemostatic effect in the following manner:

(1) The cellulose fiber possesses excellent absorption by tissue fluid such as blood and rapidly dissolves when contacting the blood;

(2) The cellulose fiber accelerates coagulation reaction of fibrin monomers converted from fibrinogen with thrombin which are contained in the soluble trauma-healing hemostatic cellulose fiber including coagulation proteins, also promoting and activating a blood clot cascade even when the blood clot cascade is low or inactive; and

(3) Cross-linking reaction of the coagulation factor XIII which is contained in the same soluble trauma-healing hemostatic cellulose fiber stabilizes the agglutinates;

4. Furthermore, the inventive hemostatic fiber enhances adhesion and aggregation of blood platelets at the wound and interacts with fibronectin which is an adhesion protein, to promote cell adhesion activity of the fibronectin;

5. The advantages provided by the present invention have been substantiated by the comparative testing presented in the Tables and Figures of the present application. This comparative testing has been carried out under my direction and control;

6. Referring to the test results documented in the various Tables and Figures of the present application, Table 1 of the present application shows ability to control degree of hydroxyl group substitution in the hemostatic cellulose fiber, namely by controlling reaction time with monochloro acetic acid in accordance with the inventive method of preparation;

7. Table 2 of the specification shows complete solubility of the inventive hemostatic cellulose fiber in water and saline, whether the coagulation protein is imparted to the fiber by spraying or chemical bonding;

8. Referring to these comparative test results in Fig. 1, the improved fibrin monomer absorptivity was attained with the inventive hemostatic fiber having the coagulation protein either applied to the surface thereof or chemically bonded thereto (plots C and D), over hemostatic fiber having no coagulation protein imparted thereto (plot B) or the absence of hemostatic fiber altogether (plot A). Thus, the methods of application clearly result in a different improved hemostatic fiber being obtained;

9. Referring to Table 3 and Fig. 2, the improved platelet agglutination activity was attained with the inventive hemostatic fiber prepared by either method (graphs C and D) over hemostatic fiber containing no protein (graph B) or the absence of fiber altogether (graph A). In fact, fiber without the protein (graph B) failed to improve over total absence of fiber (graph A);

10. Table 4 shows the improved adhered cell count was also attained with the inventive fiber prepared according to either method over fiber containing no protein and the complete absence of fiber;

11. Test results presented in Table 5 show hemostasis can be achieved with the inventive fiber in as little as 10-11 seconds on average as opposed to fiber not containing protein (which took 33 seconds on average) or the absence of fiber altogether;

12. The improvements documented in the Tables and Examples of the present application are surprising and synergistic, not at all expected by the level of skill in the art available to me;

13. Soe et al., Colombo et al., Edwardson et al., and Sugitachi et al. fail to suggest to me, one skilled in the art, the features of the inventive hemostatic fiber and accompanying advantages which have been documented in the comparative testing, for the following reasons;

14. More particularly, Soe et al. disclose a tissue sealant comprising a combination of thrombin, fibrinogen, carboxymethylcellulose (CMC) or alkali metal or alkaline earth metal salt thereof which is prepared by admixing thrombin and CMC with fibrinogen (page 3, lines 30-35) or adding the CMC to a fibrinogen followed by adding a thrombin, or alternatively adding CMC to fibrin adhesive (page 4, lines 2-7). Examples 1 and 2 at page 5, lines 15-51 of Soe et al. describe preparing lyophilized CMC powder which is then added to a fibrin adhesive. Accordingly, Soe et al. fail to suggest to me, one skilled in the art, preparing a fiber for wound-healing benefit, much less a fiber imparted with coagulation protein in the fashion of the present invention;

15. Colombo et al. merely relate to etherification of cellulose fibers ultimately used in products such as sanitary towels or napkins, bandages, tampons, etc (column 7, lines 1-2). In fact, an explicit goal of Colombo et al. is preparing hydroinsoluble carboxy-alkyl cellulose (column 1, lines 43-48) for use in the sanitary towels, napkins, bandages, etc. which clearly should not be water-soluble. Accordingly, Colombo et al. actually teach away from making the present invention to me, one skilled in the art;

16. Edwardson et al. just contain a general disclosure that a thrombin-like enzyme can be immobilized upon a support such as cellulose or derivatives. Thus, Edwardson et al. neither disclose nor suggest to me, one skilled in the art, preparing an etherified cellulose fiber as in the claimed invention with the coagulation protein imparted in the inventive fashion to thereby attain the advantageous improvements documented in the present application;

17. Finally, Sugitachi et. al merely disclose fixing blood coagulation factor XIII to a variety of structures such as sutures, pads, bandages, etc. formed from a variety of materials, such as carboxymethycellulose (column 1, line 49- column 2, line 5). Sugitachi et al. neither disclose nor suggest preparing the claimed etherified cellulose fiber with all three coagulation proteins imparted thereto. Furthermore, the materials disclosed in Sugitachi et al. are not intended to be water or blood-soluble, hence teaching away from the

invention claimed herein to me, one skilled in the art;

18. Accordingly, even if Soe et al., Colombo et al., Edwardson et al., and Sugitachi et al. are combined, the features of the claimed invention together with the accompanying advantages would still not be suggested to me, one skilled in the art. The surprising synergistic advantages provided by the claimed invention have been documented in the extensive comparative testing presented in the present application; and

19. All statements made herein of my own knowledge are true and all statements made on information and belief are believed to be true; and further these statements are made with knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and such willful false statement may jeopardize the validity of the application or any patent issued thereon.

May 26, 2004
Date

Yoshio Jo
Yoshio Jo

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